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The surprising problem of unavailable medicines

On the eve of Finland's EU membership eight and a half years ago, no one would have believed that one of the results of becoming a member would be the unavailability of medicines. Nevertheless, this is now the case.

Medicines are authorised for the market through quicker and more efficient marketing authorisation processes. Nonetheless, medicines do not necessarily make their way to the pharmacy shelves or to the customers. Naturally, the patients and all of health care suffer the consequences, but it also signifies a waste of expert resources and administrative idling.

Still in 1993, all the authorised medicines were, practically speaking, available on the market. In those days, the Medicines Act required that a medicinal preparation had to be placed on the market within a year of marketing authorisation being granted. Failing this, the authorisation expired. The price of the medicinal preparation was negotiated to a reasonable level already by the time the authorisation was granted.

In May 2003, there were 4,700 nationally granted marketing authorisations in force in Finland. Only 77 per cent of these products were placed on the market in Finland. As of 1995, 700 marketing authorisations have been issued centrally in the EU, but even fewer of these – only about 40% – are available in Finland. It is also extraordinary that pharmaceutical companies, more often than before, apply first to the Finnish National Agency for Medicines for marketing authorisation, using Finland as a so-called Reference Member State, but of the medicinal products concerned (about 260 marketing authorisations, mainly for generic preparations) only a fifth have been placed on our market.

The availability problem affects all kinds of medicines. As examples we could mention the hypertension medicine (irbesartan + hydrochlorothiazide) that received marketing authorisation in 1998, the arrhythmia

medicine (dofetilide) that received marketing authorisation in 1999, and the implant (rhBMP-2) used in the treatment of shinbone fractures that received marketing authorisation in 2001, in addition to a host of generic preparations. Whatever opinion one might have of the therapeutic value of products on the 'haven't got' list, the current situation is not acceptable. What is the point of maintaining an administratively demanding advance-control system of a high level of expertise and efficiency, if products do not, in fact, come into use?

There are, to be sure, many reasons for the situation that has arisen. They may be related to the small size of the Finnish market and the consequent profitability estimates. Every product placed on our market must have the appropriate packaging and patient information leaflet in Finnish and Swedish. Apart from that, the reason may be – at least from the pharmaceutical industry's point of view – the problem related to the pricing negotiations for purposes of admittance into the drug reimbursement system in general, and to a special reimbursement category in particular. The problem is exacerbated by there being insufficient obligations or incentives to place medicines on the market. Current 'desirability paragraphs' of the Medicines Act do not appear to suffice. It is true that the EU's medical legislation review package contains a recommendation for obligatory placement of medicines on the market, but in a more lenient form than previously applicable in Finland.

The authorities do not have sufficient means to actively promote the placing of medicines on the market. In any case, the causes of the problem should be studied. The Finns have the right to assume that medical innovations approved by the EU, or generic medicines approved by the Finnish National Agency for Medicines, would be normally available here as well.

Summary

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Treatment of neuropathic pain

Neuropathic pain, i.e. pain caused by damage to neural tissue, is traditionally considered a condition difficult to treat. Nevertheless, several drugs are available which have proven effective in controlled clinical trials. The best medication for each patient is found through individual trials of various therapies. Tricyclic antidepressants, carbamazepine, gabapentin and tramadol may be tried in primary health care. In complex situations it may be worthwhile considering referring the patient to a pain clinic for treatment assessment.

The definition, prevalence and diagnosis of neuropathic pain

According to the definition of the International Association for the Study of Pain, neuropathic pain, i.e. pain caused by damage to neural tissue, is a pain condition caused by damage to, or a functional disorder in, the pain transmitting nerve system (1). The term “neurogenic pain” is used when the functional disorder is reversible, as distinct from a condition of neuropathic pain, indicating a permanent abnormality. The neuropathic pain conditions are distinguished according to the site of the lesion: central or of CNS origin (e.g. a pain condition following a cerebrovascular accident), peripheral or of peripheral nervous system origin (e.g. diabetic neuropathy, pain after neural tissue damage), or a combination of these (e.g. post-herpetic neuralgia).

It is estimated that about one percent of the UK population suffers from neuropathic pain conditions, and it is therefore a rather common complaint for which doctors need to find appropriate treatment. About 8% of patients who have had a cerebral infarct, 28% of MS patients, and a minimum of 50% of patients with spinal cord injury suffer from neuropathic pain.

According to a Finnish study, 8% of patients with adult type diabetes have peripheral polyneuropathy

at the time of diagnosis, the most common symptoms of which in addition to pain are numbness and lack of sensation (2). About 5% of patients with peripheral nerve damage develop pain caused by neural tissue damage. Animal studies show that proneness to the development of a condition of neuropathic pain following peripheral nerve damage is determined by hereditary factors.

The diagnosis and treatment of neuropathic pain are based on the location of the pain and the logical neuroanatomical localisation through signs and symptoms indicating abnormal function of the tactile sense (e.g. in the region innervated by a nerve branch or root), and the identification of the cause of the damage. The symptoms may include continuous pain, scintillating pain resembling an electric shock, allodynia, i.e. a condition in which a normally painless stimulus is transformed into pain, and various abnormal sensations such as paraesthesia and dysaesthesia. The tactile sense may be exaggerated or impaired depending on the quality of the sensation. If the diagnosis is evident (post-herpetic neuralgia, for example), no further examinations are necessary following the taking of a good past medical history and examination of the status of the patient. Depending on the individual

case, however, it may be advisable to use imaging, laboratory and neurophysiological examinations to establish the cause of the symptoms and the options for treatment, depending on the cause. In neuropathic pain, however, it is only rarely possible to deal with the cause, and treatment is therefore symptomatic.

The mechanisms of neuropathic pain have not yet been fully established. The plasticity of the nervous system, i.e. its ability to undergo functional and structural changes in association with various disease processes, is a key issue in the development of neuropathic pain conditions. In conditions of peripheral neuropathic pain, increased formation of impulses has been found in the pain nerve ends, axons and sensory ganglia. This is at least partly due to the increased number of sodium channels in the cell membrane of the nerve. Another prominent characteristic of neuropathic pain is the relative weakness of central inhibitory mechanisms. Sensitisation also occurs at that level of the central nervous system where the activation of NMDA receptors plays a central role. Drugs used for the treatment of neuropathic pain have several different mechanisms of action which are logical in view of the pathophysiological mechanisms (Table 1).

Treatment of neuropathic pain

In some patients the symptoms may be so mild as merely to need a diagnosis and an explanation of the mechanisms of the symptoms and the character of the pain. Neuropathic pain is not a warning sign of anything; instead, it is a nuisance produced by a damaged sensory path. Exacerbation of symptoms as a result of various stimuli is not a sign of further damage. The patient is encouraged to avoid those situations which most exacerbate the symptoms and to look for alternative courses of action, the aim being activity and a good quality of life in spite of the symptoms. If the pain causes disruption to the patient's everyday life, it is justified to try some medical treatment. According to a meta-analysis, the alleviation of pain can be considered good if a 30% reduction in neuropathic pain is obtained or a minimum reduction of two numbers in the scale of severity of pain from 0 to 10 (3). A minimum of 50% pain relief, i.e. the criterion used in the NNT (number needed to treat) calculations, indicates very good alleviation of pain (3, 4).

The choice of medication depends on the patient's previous experience of drugs available on the market, other diseases and associated medication, motivation to try the suggested medication, the price of the drug and the symptom picture. If the most difficult symptom is a scintillating pain resembling an electric shock, the first line of treatment is carbamazepine. It is recommended that hyperaesthesia following herpes zoster in elderly patients with a multitude of illnesses be treated with lidocaine ointment as a first choice. Dosage recommendations for each drug are detailed in Table 2. If even after a dose adjustment the efficacy of the drug being tried is not sufficient according to the patient's own judgment, the first drug is withdrawn and replaced by another one for the patient to test. After experimenting with some monotherapies, combinations of drugs with various mechanisms of action can be tried. Complex polypharmacy ought, however, to be avoided.

Table 1. Mechanisms of action of drugs used for the treatment of neuropathic pain.

<i>Tricyclic antidepressants</i>	<i>serotonin and noradrenaline effect</i>
<i>Carbamazepine</i>	<i>sodium channel blockade</i>
<i>Oxcarbazepine</i>	<i>sodium channel blockade</i>
<i>Tramadol</i>	<i>serotonin and noradrenaline effect, μ-opioid agonism</i>
<i>Gabapentin</i>	<i>calcium channel blockade</i>
<i>Lamotrigine</i>	<i>sodium channel blockade, inhibition of glutamate release</i>
<i>Oxycodone</i>	<i>μ-opioid agonism</i>
<i>Topical lidocaine</i>	<i>sodium channel blockade at the nerve ends</i>

Tricyclic antidepressants

Tricyclic antidepressants are the corner stone of neuropathic pain treatment. Their efficacy is proven in both central and peripheral neuropathic pain conditions (4). Considerable differences in efficacy between different drugs have not been found, but nortriptyline is better tolerated than amitriptyline (5). Alleviation of pain is independent of the effect of the mood, its onset is more rapid and relief can be attained at lower doses. As the patient's sleep is often disturbed, the first effect to be desired of the drug is undisturbed sleep at night. The total benefit can be assessed once the drug has been used for a couple of weeks without changing the level of the dosage. Since the metabolism of tricyclic antidepressants varies extensively between individuals, specifications for concentrations are recommended if the patient exhibits undesirable effects even at low doses, or if there is no response at daily doses as high as 150 mg. While the concentration is being monitored, the dose may be increased by titration as necessary if the drug is well tolerated by the patient. The most common undesirable effects include tiredness, dryness of the mouth, constipation, disturbances of micturition and orthostatic hypotension. Weight problems, disturbances of sexual functions and arrhythmias may occur. The blood dyscrasias are rare. To avoid sedation the drug should be taken early on in the evening before going to bed. Dryness of the mouth can be relieved by topical sialagogues, and constipation can be treated by laxatives which increase the bulk of the

intestinal contents. The patients with narrow-angle glaucoma, prostatic hyperplasia or heart disease should be treated with caution.

Antiepileptic agents

Carbamazepine is the drug of choice in trigeminal neuralgia; it brings relief to about 70% of the patients. It has also been found effective in other conditions of neuropathic pain (4). The same dosage regimes are applied as in epilepsy, and the serum drug concentration can be established as necessary. Blood count and liver values should be monitored, especially at the start of treatment. The most common adverse reactions include tiredness, vertigo and hyponatraemia. Liver-enzyme-induced interactions with many drugs, including combined oral contraceptives, should be borne in mind. Carbamazepine and oxcarbazepine are equally effective in trigeminal neuralgia (6). Oxcarbazepine is better tolerated than carbamazepine, but it is recommended that the serum sodium level be monitored at the beginning of the treatment to exclude the possibility of hyponatraemia.

Gabapentin is effective in the treatment of pain caused by diabetic neuropathy, post-herpetic neuralgia and phantom pain (7-10). The absorption of gabapentin is saturating and it has no pharmacokinetic interactions with other drugs as it is not metabolised in the liver but it is completely excreted via the kidneys. Due to its safety of use and efficacy, along with tricyclic drugs gabapentin is considered as first line treatment in the neuropathic pain conditions mentioned above.

Gabapentin is administered three times a day, and the target dose in the treatment of pain is 900–3,600 mg/day. The response to treatment can be assessed within a couple of days of reaching the target dose. The most common adverse reactions are vertigo, tiredness and oedema.

The efficacy of lamotrigine is proven in conditions of both central and peripheral pain (11-15). The dose is increased very slowly to avoid rash. Monitoring by laboratory tests is not necessary, and adverse reactions of CNS origin are fewer than with conventional antiepileptic agents. Due to the slow titration of the dose, the use of lamotrigine is restricted to the cases where drugs with easier administration have not brought adequate relief.

Opioids

The effect of tramadol is exerted via both the opioid receptors and the serotonin and noradrenaline systems. Tramadol, classified amongst the weak opioids, causes distinctly less dependence and tolerance than strong opioids do. Its efficacy is proven in conditions of polyneuropathic pain and post-herpetic neu-

ralgia (16-18). The most common adverse reactions include nausea, vertigo, tiredness and headache. Interactions with antidepressants should be kept in mind in the administration of tramadol; serotonin syndrome and elevated concentrations are possible (19).

Pure opioids were previously considered to have no effect on neuropathic pain, but a proportion of patients with neuropathic pain were later shown to benefit from their use. Oral oxycodone with long-term effect is proven to be effective in both post-herpetic neuralgia (20) and conditions of diabetic neuropathic pain (21). The doses used in the studies were relatively small, 20-80 mg/day. The most common adverse reactions include tiredness, constipation and pruritus. The status of strong opioids in the treatment of neuropathic pain remains unsettled, since only a proportion of patients benefit from these drugs and because of the dependence strong opioids may cause. As a rule, introduction of strong opioid therapy for other than cancer pain is the responsibility of special clinics. Before starting opioid therapy it is necessary to know the patient, to be

truly familiar with the effects of opioids, and to know how to carry out the treatment and how to make a correct selection of patients. The dose is slowly increased by titration and by monitoring the response and any possible adverse reactions. The use of a laxative which increases the bulk of the intestinal content is recommended to be introduced at the start of the opioid therapy. If significant pain relief is not obtained by the opioid, the drug is slowly withdrawn by gradually decreasing the dose.

Topical lidocaine

Topical lidocaine, both in gel and plaster format, is found effective in post-herpetic neuralgia if the patient has dynamic mechanic allodynia, i.e. light touching of the skin is painful. The effect is based on the sedation of overactive nerve end function (22-23). In Finland, both the lidocaine ointment and the lidocaine plaster are preparations for compassionate use. The ointment is applied three times a day on to skin sensitive to touch. The use of plaster for 12 hours a day provides an effect for 24 hours.

Table 2. Administration and dosage of drugs for neuropathic pain

<i>Drug</i>	<i>Initial dosage</i>	<i>Titration of dose</i>	<i>Maximum recommended daily dose*</i>
<i>Tricyclic antidepressants</i>	<i>10–25 mg at night</i>	<i>10–25 mg in increments every 3–7 days</i>	<i>150 mg or according to concentration</i>
<i>Carbamazepine depotpreparation</i>	<i>100 mg x 2</i>	<i>100 mg in increments every 3–7 days</i>	<i>according to concentration</i>
<i>Gabapentin</i>	<i>300 mg at night</i>	<i>300–900 mg in increments every 1–3 days, taken 3 times daily</i>	<i>3,600 mg*</i>
<i>Lamotrigine</i>	<i>25 mg x 1</i>	<i>25–50 mg in increments, every 1–2 weeks, taken twice daily</i>	<i>400 mg*</i>
<i>Tramadol</i>	<i>50 mg x 1</i>	<i>50 mg in increments, taken 3 times daily, depotpreparation twice daily</i>	<i>400 mg</i>
<i>Oxycodone</i>	<i>10 mg x 2</i>	<i>10 mg in increments every 1–3 days, taken twice daily</i>	<i>80 mg*</i>

* the maximum dose used in studies on neuropathic pain

Conclusion

Even though new appropriate drugs have been introduced in recent years for the medical treatment of neuropathic pain, we are nowhere near achieving reasonable control of pain in all patients. Dorsal column stimulation of the spinal cord may be useful in these cases if one is dealing with peripheral neuropathic pain. On-going research in the field is extensive and novel preparations are expected to figure on the market in the near future. As knowledge of the mechanisms of neuropathic pain becomes more specific, it will be possible to develop drugs based on the newly found mechanisms of action. In practical work it is worth bearing in mind that the support shown by the physician towards his/her patient is especially important when the benefit of medical treatment remains modest. If a good response is obtained, occasional appointments for the evaluation of the condition and renewal of the prescription are recommended as with the treatment of any chronic disease

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Summary

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Thirty years of adverse drug reaction monitoring in Finland

The purpose of an ADR register is to identify any new risks associated with the use of drugs. The rarer the adverse reactions, the better the register works as a tool for their identification. The information made available through the reports on common adverse reactions is nevertheless difficult to interpret. Many of the more common reactions also occur in patients who have not even received the drug, which often makes it difficult to establish the extent of the effect of the drug exhibited in the reaction produced.

The reporting of adverse drug reactions is done on a voluntary basis in Finland, whereas in Sweden and Norway, for example, it is mandatory to report any adverse reactions. The mandatory reporting does not necessarily improve the register, because voluntary reporting may produce reports better in quality rather than a larger number of reports. Significant under-reporting also occurs in countries where it is mandatory to report (1, 2).

Despite the voluntary reporting system in Finland, the National Agency for Medicines hopes that all suspected adverse reactions will be reported. It is especially advised that serious adverse reactions caused by drugs, including fatalities, life threatening reactions, reactions requiring hospitalisation or prolongation of the hospital stay, reactions causing continuous functional defect or impairment of functional ability,

and reactions causing congenital anomalies or abnormalities, should be reported. It is also advised to report all drug interactions, including adverse reactions to new medicinal products which have been available on the market for less than two years, increased frequency of a suspected adverse reaction and unexpected adverse reactions the character and seriousness of which differ from those listed in the SPC. It is advisable to report even already known adverse reactions. In this context, it should be emphasised that a mere suspicion of a possible adverse reaction is sufficient reason for submitting an ADR report.

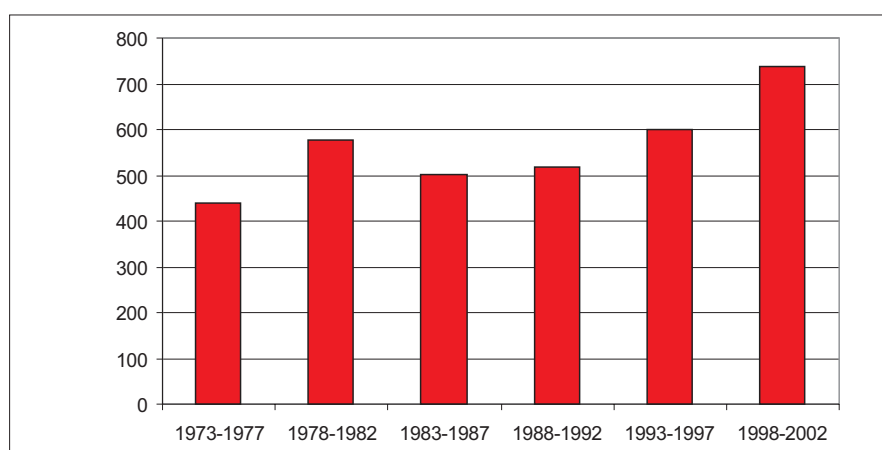
ADR reports

The annual number of reports on adverse drug reactions in recent

years has been around 700–800 (Fig. 1). The proportion of serious reactions among these reports is about 50%. This is nevertheless only a fraction of the real number of significant adverse reactions.

The most important groups of drugs figuring in the reports include antimicrobials, drugs affecting the nervous system, and drugs for the treatment of diseases of the cardiovascular system and of the musculoskeletal system (Table). One symptom at least in about a quarter of the ADR reports consisted of various skin reactions; other common symptoms of adverse reactions comprised various general symptoms, adverse reactions of the blood count, the gastrointestinal tract, the respiratory organs and the nervous system (Fig. 2).

Fig. 1. The number of ADR reports in Finland 1973–2002



Report evaluation

ADR reports submitted to the National Agency for Medicines are discussed on a weekly basis at expert meetings, where the evaluation of causality in the submitted reports and an assessment of the seriousness are made. The majority of the ADR reports contain information given by a doctor to the Agency about the reaction. The marketing authorisation holder of the drug receives a copy of the report, without personal details of the patient, on both serious and non-serious reactions caused by the drug. If the reporting doctor wishes his/her details to remain confidential and their availability to be restricted only to the National Agency for Medicines, then the information given in the report is sent to the marketing authorisation holder anonymously without the name or contact details of the doctor. Doctors may also report to the marketing authorisation holder directly who then, within 15 days of the report, is required to report to the National Agency for Medicines all the serious adverse reactions which have occurred in Finland.

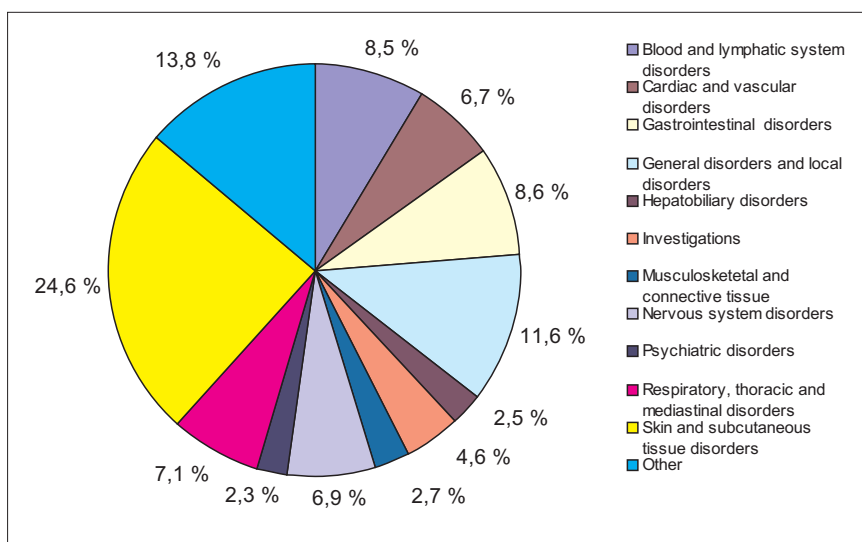
The reports on serious ADRs received by the Agency are reported to the EMEA, other EU member states and the WHO database.

A large number of common adverse reactions are detected early on in the drug trials designed and carried out for new drug development and marketing authorisation purposes. Prior to the approval of a marketing authorisation, a new drug has nevertheless only been tested in a maximum of a couple of thousand patients. Consequently, rare adverse reactions which occur in less than one in a thousand recipients are often not detected in these clinical studies. Experience of the risks associated with long-term treatment is also limited prior to the approval of a marketing authorisation. It is nevertheless unreasonable to require considerably more extensive trials than at present for the approval of a marketing authorisation, because they would delay and prevent the development of new and necessary drugs and they could delay the most effective treat-

Adverse reactions of various drugs reported to the ADR Register of the National Agency for Medicines during 1973–2002 (percentage of the reported drugs)

<i>Drugs for diseases of the gastrointestinal tract and for metabolic diseases</i>	5%
<i>Drugs intended for diseases of the blood and blood forming organs</i>	2%
<i>Drugs used in diseases of the cardiovascular system</i>	17%
<i>Dermatologicals</i>	2%
<i>Drugs aimed at diseases of the genito-urinary and sex hormone systems</i>	5%
<i>Hormonal preparations (excluding sex hormones)</i>	1%
<i>Anti-infectives</i>	28%
<i>Antineoplastic and immunomodulating agents</i>	3%
<i>Drugs for diseases of the musculoskeletal system</i>	11%
<i>Drugs affecting the nervous system</i>	19%
<i>Antiparasitic products, insecticides and repellents</i>	1%
<i>Drugs for diseases of the respiratory system</i>	3%
<i>Drugs for diseases of the sensory organs</i>	1%
<i>Other</i>	2%

Fig. 2. The division of ADR reports by organ groups during 1973–2002



ment of diseases. Adverse reactions with a smaller frequency than 1:10,000 may also be significant, especially if they are caused by drugs which are widely used. In practice, the detection of this type of rare adverse reactions will not be possible until the drug has been in general use for years. Patients in potential risk groups are often filtered out before clinical trials, but after the approval of the marketing authorisation the use of the drug is often extended to these patient groups as well. Reporting of ADRs covers all drug consumers in need of actual treatment, and this makes the detection of adverse reactions in the risk groups easier. For the same reason, various problems associated with drug interactions are often not detected until the drug is actually used in a particular therapy.

A suspected association between the drug therapy and symptoms and findings constitutes an adequate basis for making an ADR report. It is important that indefinite suspicions and unusual observations are also reported. In individual cases it is almost impossible to demonstrate a causality relationship. However, if independent observations are received from various sources, it may reinforce the suspicion of a new adverse reaction caused by a drug.

The ADR register is a poor tool for the quantitative evaluation of ADRs because the reports received are made on varying grounds and represent an unknown proportion of the ADRs occurring in real life. According to studies, under-reporting is more common in association with non-serious and familiar reactions than with serious and unex-

pected reactions (1, 2, 3), and, it is consequently the detection of new and serious signals which represents the most important value of ADR reports.

Comparisons of safety between different drugs should be made especially carefully if they are based on the information available in the ADR register. The number of reports on a particular drug varies over different periods of time, depending on the extent to which the drug is used, its novelty value, publicity and other factors which are not associated with the effect of drug. The number of reports on adverse reactions caused by a new drug during the first years of marketing is multifarious in comparison with that in subsequent years. News in the mass media about adverse drug reactions may also increase the reporting of reactions.

The information available in the ADR register cannot be considered comprehensive as to its quantity and quality, and, consequently, further details are required to reinforce the safety signals generated on the basis of the information, for example, by establishing the causality relationship of the drug to the adverse reaction and its frequency.

Well-designed epidemiological studies are one way of obtaining further information. Such studies can provide assessments of the occurrence of the adverse reaction and comparative information on risks between different drugs. Preclinical studies can be used to establish the mechanism by which any adverse reaction is generated.

After the assessment, if any reaction appears to be new and significant, measures can be taken to pre-

vent any further adverse reactions. These measures include, for example, the inclusion of the reaction and the associated warnings and precautions in the product information (the SPC and the PIL). Other measures could include the stipulation of a restriction for use, e.g. changing the OTC status of a drug to a prescription only drug, or restricting the therapeutic indications and user groups of the drug. Information bulletins published on the website of the National Agency for Medicines (www.nam.fi), or health care professional (dear doctor) letters, can be used for attracting the attention of doctors. In extreme cases, the product may be suspended, and the marketing authorisation may be withdrawn if necessary. The final discussion of any significant measures associated with safety usually takes place at the CPMP; its evaluation then leads to a Commission decision which is binding to all EU member states.

Literature

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Summary

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Classification issues

A medicine is a preparation or a substance the purpose of which, when used either internally or externally, is to cure, alleviate or prevent a disease or the symptoms of a disease in humans or animals. A preparation or a substance used either internally or externally to establish the condition or the cause of a disease, or to restore, improve or change the physiological function in humans or animals, is also considered to be a medicine (Section 3 of the Medicines Act).

The National Agency for Medicines has published a list as a guideline on the substances which are to be considered medicines (<http://www.nam.fi/english/laws/classification/medicine-list/index.html>). The substances listed in appendix 1 and the herbals listed in appendix 2 can be considered medicines. The substances and herbals are listed in alphabetical order in the list together with their Latin, Finnish and Swedish names.

Other substances and herbals used in accordance with Section 3 of the Medicines Act and with a medicinal purpose comparable to that of substances listed in appendix 1 or herbals listed in appendix 2 can also be considered medicines. Preparations and substances used for medicinal purposes can also be classified as medicines without regard to their form, composition, manufacturing method or mechanism of action, which may be dissimilar to those of conventional medicines. These include radioactive pharmaceutical preparations, allergen preparations and medicinal gases.

Preparations having daily doses containing vitamins or minerals in excess of the amounts indicated in appendix 3 of the list of medicines

can also be classified as medicines. Vitamin and mineral preparations intended for children are considered medicines.

The list of medicines is confirmed every three years. The list was last confirmed in 2000, which means that the next list of medicines will be published this year.

Classification of medicines

According to the Medicines Act, it is the responsibility of the National Agency for Medicines to determine whether a substance or a preparation should be considered a medicine. The classification is established for each product individually the product being classified either as a medicine, a non-medicine or a medical device. The classification is dependent on both the composition of and the therapeutic use for the product. The product is classified as a medical device if it fulfils the criteria defined in the legislation (Act on Medical Devices 1505/1994).

Written request

A signed application for classification is required for a product to be classified (an application by e-mail is not valid). The application for classification including enclosures should contain the following details

- the name of the preparation
- precise qualitative and quantitative composition
- proposed therapeutic use
- pictures of packages
- any information of classification category in another country

The application for classification should include full contact details of

the applicant in case any further information.

The decision on classification is obtainable on payment of EUR 85 within about 1–2 months of submitting the application. The decision will be sent in writing to the applicant.

After the decision

Once the product is classified as a medicine, it may not be sold as a foodstuff or as a grocery item. A marketing authorisation is subsequently applied for where a product classified as a medicine. Information on marketing authorisation applications is available on the website of the NAM http://www.nam.fi/english/control/marketing_authorisation/index.html. The manufacturer is responsible for the sale and the choice of an appropriate channel of sale. It is the duty of the manufacturer also to ensure that a preparation classified to be sold at pharmacies is withdrawn from the shops selling health food products.

Guidelines on the marketing and launching medical devices are to be found on the website <http://www.nam.fi/english/devices/index.html>

More information on website

Information on issues associated with the classification of medicines is available on the Agency's website <http://www.nam.fi/english/laws/classification/index.html>

The classification of a product does not, however, mean that marketing authorisation would have been obtained for the product.

Translation Mervi Moisander